

Extracellular α -synuclein alters synaptic transmission in brain neurons by perforating the neuronal plasma membrane

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© 2015 International Society for Neurochemistry. It has been postulated that the accumulation of extracellular α -synuclein (α -syn) might alter the neuronal membrane by formation of 'pore-like structures' that will lead to alterations in ionic homeostasis. However, this has never been demonstrated to occur in brain neuronal plasma membranes. In this study, we show that α -syn oligomers rapidly associate with hippocampal membranes in a punctate fashion, resulting in increased membrane conductance (5 fold over control) and the influx of both calcium and a fluorescent glucose analogue. The enhancement in intracellular calcium (1.7 fold over control) caused a large increase in the frequency of synaptic transmission (2.5 fold over control), calcium transients (3 fold over control), and synaptic vesicle release. Both primary hippocampal and dissociated nigral neurons showed rapid increases in membrane conductance by α -syn oligomers. In addition, we show here that α -syn caused synaptotoxic fail